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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/783,092

02/23/2004

Taru Blom

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EXAMINER

GEMBEH, SHIRLEY V

ART UNIT

PAPER NUMBER

1614

MAIL DATE

DELIVERY MODE

05/28/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/783,092	Applicant(s) BLOM ET AL.	
	Examiner SHIRLEY V. GEMBEH	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 February 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3,4 and 7-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3,4 and 7-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>2/19/08</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The response filed **2/19/08** presents remarks and arguments to the office action mailed **11/19/07**. Applicant's request for reconsideration of the rejection of claims in the last office action has been considered.

Applicant's arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of Claims

Claims 1, 3-4 and 7-13 are pending in this office action.

Claims 1, 7, 9-11 are amended and claims 2 and 5-6 are cancelled.

Allowable Subject Matter as state is the last office action is withdrawn due to the below rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

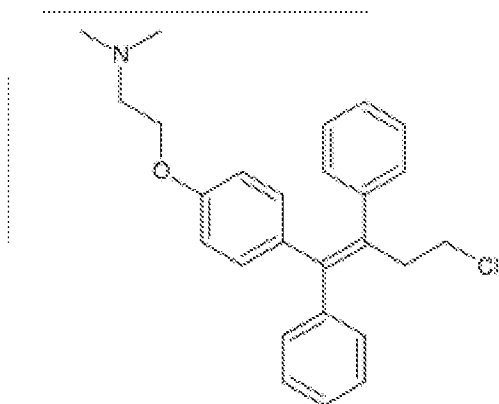
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invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-4 and 7-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marttunen et al., Calcified Tissue International, 65:365-368 (1999) taken with Kangas, Cancer Chemotherapy and Pharmacology, 27:8-12 (1990) in view of Fukumitsu et al. Metabolism 51(7), 814-818, 2002 (new) and Lindberg et al. Journal of Endocrinology (2001) **171**, 229-236 (new) and Suda et al. The Journal of Immunology, 2004, 172: 2504-2510 (new) and Crofton et al. Clinical Chemistry 49, No. 1, 2003 (new)

Marttunen et al. teach administration of toremifene



Toremifene

having a core structure that is the same as the claimed compound of formula I, to ascertain bone resorption in postmenopausal breast cancer patients by measuring bone resorption markers, as required by instant claims 1, 3 and 4. See abstract, underlining. With regard to claim 5, the reference suggests bone an increase bone turnover is detected an obvious variation of claims 12 and 13. See abstract and page 367, underlining. The reference however, fails to teach the exact claimed compound of instant claim 1. Marttunen teaches the administration of toremifene as 40 mg/day. See abstract as required by instant claims 14 and 18. The reference fails to teach the specific bone markers recited in instant claim 1 and the specific concentrations of the compound 30, 60 and 90 as required by instant claims 15-17 and 19-21.

Kangas teaches different forms or metabolites of toremefine as TORE, TORE II, V, IV etc. See page 9, Fig. I.

Fukumitsu et al. teach a diagnostic potential of bone resorption marker, type I collagen-cross-linked N telopeptide in urine, wherein the bone resorption is atleast 65

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nm/mmol creatine. See underlining as required by instant claim 1 in part, 7-8. The reference also teach one of ordinary skill in the art to use carboxy terminal propeptide of type I procollagen as an assessment tool in determining bone resorption. See underlining, pg, 814.

Suda and Lindberg are used here as one to show that bone resorption assays are determined by the using markers such as tartrate-resistant acid phosphatase as in instant claim 10. Even though no mention of the subtype was taught one of ordinary would be motivated to use any subtype for assessing bone resorption as the use of thers has not been shown that it won't result in the same information as that of the subtype 5b. It is also inclusive that the subtype 5b is used based on not identifying any subtype in the reference.

Crofton et al teach the use of a marker Crosslaps measured in both serum and urine in children and post menopausal women.

One of ordinary skill in the art would have been motivated to administer TORE VI, which is the same as the claimed compound of formula I to patients suffering from increased bone turnover known as bone loss. Therefore, one of ordinary skill in the art would have been motivated to administer a metabolite of toremifene such as ospemifene (compound of formula I) as claimed and taught as TORE VI to patients with increased bone loss. Kangas teaches the metabolites of toremifene to be biologically active and to resemble toremifene in its hormonal effects. It would have been reasonable to expect a decrease in bone loss because Kangas reference teaches toremifene metabolites are inclusive of ospemifene.

As to the varying concentration the determination of a dosage having the optimum therapeutic index is well within the level of the ordinary skill in the art, and the artisan would be motivated to determine the optimum amounts to get the maximum effect of the drug, hence the reference makes obvious the instant invention.

With regards to combination of Crosslaps and TRAP5b, one of ordinary skill would have been motivated to use both assaying methods to determine bone resorption in patients because both assays are determine from serum. Also, the instant situation is amenable to the type of analysis set forth in *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order form a third composition that is to be used for the very same purpose since the idea of combining them flows logically from their having been individually taught in the prior art. Applying the same logic to the instant process claims, given the tdiagnosing bone resorption, it would have been obvious to use both compounds as a diagnostic tool because the idea of doing so would have logically followed from their having been individually taught in the prior art.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976).

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

No claim is allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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5/20/08

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614